

## REMARKS

**Amendments to the Specification**

Applicants have amended the specification to incorporate the sequence listing into the application. The sequence listing is submitted herewith via EFS, in compliance with 37 CFR§1.52(c)(5). The sequence contains no new matter. It is respectfully requested that the sequence listing be incorporated into the application.

**The Sequence Listing**

Applicants have enclosed a new sequence listing and request its entry in place of the previously entered sequence listing. The sequence adds SEQ ID NO:709. SEQ ID NO:709 represents GenBank entry NM\_012104. The version of NM\_012104 appearing in the sequence listing as SEQ ID NO:709 appeared in GenBank on November 2, 2000 and is included in the U.S. Provisional patent application No. 60/363,124 priority application (see, Table III, page 351). The sequence listing adds no new matter and applicants respectfully request its entry.

**Amendments to the Claims**

Claims 1 and 3 have been amended, claims 2, 4-36 have been canceled, and new claims 37-59 have been added. These amendments and additions are fully supported by the application as filed. To expedite prosecution representative support from the instant application and various priority applications for all claims currently pending is provided in the following table.

Claim No.	Support from U.S. Appl. No. 10/607,933	Support from PCT/US03/05028	Support from U.S. Appl. No. 60,363,124
1	7:12-22, 7:29-8:3, 8:8-31, 9:5-6, 10:7-14, 10:28-11:7, 12:1-6, 12:15-26, 14:1-7, 17:7-14, 17:17-20, 19:8-17, 21:26-22:23, 125, Tables III & IV, Fig. 4 & 5	8:15-19, 8:21-30, 9:1-5, 9:6-13, 9:20-26, 10:4-11, 10:13-15, 12:13-15, 13:3-6, 14:3-10, 14:19-24, 16:26-17:27, 23:15-20, 28:3-23, 29:3-20, 29:28-30:10, Tables I, IV and V, Fig. 18	3:15-17, 5:14-17, 10:3-11:25, 12:4-9, 18:1-5, 19:11-14, 24:15-22, 35:29-30, Table I & III
3	13:1-2, Figs. 4 & 5	8:21-22, 30:2-4, Tables I and IV, Fig. 18	35:29-31, Table I

<b>Claim No.</b>	<b>Support from U.S. Appl. No. 10/607,933</b>	<b>Support from PCT/US03/05028</b>	<b>Support from U.S. Appl. No. 60,363,124</b>
37	14:7-10, 14:13-15, 17:22-24, 21:27-22:23, 34:18-22, 24:29-37:3	16:26-16:26, 27:28-28:2	6:19-7:11, 5:14-17, 10:3-11, 17-25
38	21:27-22:23, 26:11-16, 34:13-18, 24:23-28, 35:4-9, 35:14-19	16:27-17:26, 22:10-12, 27:23-28	6:19-7:11, 10:1-30
39	14:21-28, 18:2-4, 26:3-5, 26:11-16, 37:21-24	20:30-31, 21:16-17, 22:2-3, 68:17-18	10:3-11, 10:17-25
40	14:27-28, 18:2-4	10:19-20, 29:13-14, 31:14-16, 86: 16-31	8:21-25, 13:18-14:9
41	21:27-22:23, 35:25-31, 36:4-10, 36:15-21, 36:27-31, 37:14-17	16:26-17:26, 28:3-9, 28:13-19, 28:24-30	6:19-7:11, 6:19-7:11, 10:3-16, 10:25-30 10:31-11:25
42	21:27-22:23, 35:31-36:3, 36:10-13, 36:31-37:3	16:26-17:26, 35:15-18	6:19-7:11, 10:31-11:25
43	21:27-22:23, 17:27-29, 36:21-24	16:26-17:26, 28:30-29:2, 35:32-36:3,	6:19-7:11, 10:31-11:25
44	15:7-9, 19:4-6, 20:3-11, 24:25-25:3	10:30-11:2, 15:3-4, 19:11-20:2, 29:23-27	8:26-9:13, 9:23-25
45	15:30-31, 18:7-8, 24:15-25:6	11:20-21, 19:11-20:2	8:26-9:13
46	14:7-10, 21:27-22:23, 26:11-16	16:26-17:26, 22:10-15, 22:27-23:2	6:19-7:11, 10:3-11, 17-25
47	21:27-22:23, 35:9-13, 35:19-23, 35:31-36:3, 36:10-14	16:26-17:26	6:19-7:11, 10:3-11, 10:17-25
48	11:24-28, 24:26-25:3	13:11-14, 19:24-25, 23:24-25, 29:23-26, 69:15-20	4:9-11, 9:7-10, 12:4-13
49	12:1-5, 14:18-20, 15:11-13, 20:8-14	14:6-10, 66:28-30,	5:13-17, Table I
50	20:21-21:16, 25:7-29	20:3-25	9:14-10:2, 11:6-11

<b>Claim No.</b>	<b>Support from U.S. Appl. No. 10/607,933</b>	<b>Support from PCT/US03/05028</b>	<b>Support from U.S. Appl. No. 60,363,124</b>
51	38:24-39:3	31:28-32:6	
52	34:58, 38:10-19, 38:24-39:3, 43:3-10, 86:27-31, Table IV	31:28-32:6, 36:17-20, 83:26-30	37:28-31
53	16:10-11, 51:9-14, 93:12-25	45:4-9, 90:12-44	45:32-46:13
54	7:12-22, 7:29-8:3, 8:8-31, 9:5-6, 10:7-14, 10:28-11:7, 12:1-6, 14:1-7, 17:7-14, 17:17-20, 19:8-17, 21:26-22:23, 26:11-16, 34:13-18, 24:23-28, 35:4-9, 35:14-19, 125, Tables III & IV, Fig. 4 & 5	8:15-19, 8:21-30, 9:1-5, 9:6-13, 9:20-26, 10:4-11, 10:13-15, 12:13-15, 13:3-6, 14:3-10, 16:26-17:27, 20:30-31, 21:15-17, 22:2-3, 23:15-20, 28:3-23, 29:3-20, 29:28-30:10, 68:16-18, Table V, Fig. 18	3:15-17, 5:14-17, 6:19-7:12, 10:3-11:25, 12:4-9, 18:1-5, 19:11-14, 24:15-22, 35:29-30; Table I & III
55	16:10-11, 51:9-14, 93:12-25	45:4-9, 90:12-14	45:32-46:13
56	7:12-22, 7:29-8:3, 8:8-31, 9:5-6, 10:7-14, 10:28-11:7, 12:1-6, 12:15-26, 14:1-7, 17:7-14, 17:17-20, 19:8-17, 21:26-22:23, 125, Tables III & IV, Fig. 4 & 5	8:15-19, 8:21-30, 9:1-5, 9:6-13, 9:20-26, 10:4-11, 10:13-15, 12:13-15, 13:3-6, 14:3-10, 14:19-24, 16:26-17:27, 23:15-20, 28:3-23, 29:3-20, 29:28-30:10, Table V, Fig. 18	3:15-17, 5:14-17, 6:19-7:12, 10:3-11:25, 12:4-9, 18:1-5, 19:11-14, 24:15-22, 35:29-30; 42:4-16, Table I & III
57	16:10-11, 51:9-14, 93:12-25	45:4-9, 90:12-14	45:32-46:13
58	43:19-44:22	37:21-38:15	15:10-26
59	43:19-44:22	27:21-38:15	15:10-26

Again, the citations provided are merely illustrative and not intended to be comprehensive.

Additional support for these claims can be found elsewhere throughout the applications.

Amendments to and cancellations of the claims are made without prejudice or disclaimer, and do not constitute amendments to overcome any prior art or other statutory rejections. They are fully supported by the specification as filed as well as various priority applications, as explained above, and thus do not introduce new matter. Additionally, these amendments and cancellations are not and should not be construed as admissions regarding the patentability of the claimed subject matter. Applicants reserve the right to pursue the subject matter of previously presented claims in this or in other appropriate patent application. These amendments add no new matter and applicants respectfully request their entry.

### **The Restriction Requirement**

The Examiner asserts that a restriction is proper between Claims 1-35 and Claim 36 as they allegedly are "related as a product and process of use" and are "distinct." Claim 36 has been canceled along with Claims 2, and 4-33. As such, it is Applicants good faith belief that the restriction requirement is moot.

Amended Claims 1 and 3 and new Claims 37-57 are directed to nucleic acid molecules that are significantly and differentially modified which target the human beta-secretase (BACE) RNA sequence, whereas Claims 58-59 are directed to methods of modulating the expression of human BACE gene using these compositions. Applicants respectfully submit that the Examiner will be doing the same search of the art whether for composition of matter claims or for method claims as the product and method claims are overlapping in scope, and do not have materially different design, mode of operation, function, or effect. Thus, the search required for examination would not be unduly burdensome. However, to the extent the Examiner believes that these sets of claims are distinct, to preclude any allegation that this amendment is non-responsive, Applicants hereby elect Claim 1, 3, and 37-57.

### **CONCLUSION**

In view of the foregoing amendments and remarks, Applicants submit that the claims are in condition for allowance, which is respectfully solicited. If the Examiner believes a teleconference would expedite prosecution, she is urged to contact the undersigned before taking further action.

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